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Abstract: Surgical revascularization remains the standard of care for many patients. Off-pump coronary artery bypass grafting (OPCAB) without cardiopulmonary bypass (CPB) has evolved during the past 20 years, and as such can significantly reduce the occurrence of neurological complications. While avoiding the aortic cross-clamping required in conventional on-pump techniques, OPCAB results in a lower incidence of stroke. However, clamp-related risk of stroke remains if partial or side-biting clamps are applied for proximal anastomoses. Others and we have demonstrated that no-touch 'anaortic' approaches avoiding any clamping during off-pump procedures via complete in situ grafting result in significantly reduced stroke rates when compared with partial clamping. Therefore, OPCAB in situ grafting has been proposed as the 'standard of care' to reduce neurological complications. However, this technique may not be applicable to for every patient as the use of free grafts (arterial or venous) requiring proximal anastomosis is often still necessary to achieve complete revascularization. In these situations, proximal anastomosis can be performed without a partial clamp by using the HEARTSTRING device, and over the last few years, considerable evidence has arisen supporting the impact of HEARTSTRING-enabled anastomosis to significantly minimize atheroembolism and neurological complications when compared with partial- or side-bite clamping. This paper provides a systematic overview and technical information about the combination of OPCAB and clampless strategies using the HEARTSTRING for proximal anastomosis to reduce stroke to levels reported for percutaneous coronary intervention.

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HEARTSTRING enabled no-touch proximal anastomosis for off-pump coronary artery bypass grafting: current evidence and technique

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Abstract

Surgical revascularization remains the standard of care for many patients. Off-pump coronary artery bypass grafting (OPCAB) without cardiopulmonary bypass (CPB) has evolved during the past 20 years, and as such can significantly reduce the occurrence of neurological complications. While avoiding the aortic cross-clamping required in conventional on-pump techniques, OPCAB results in a lower incidence of stroke. However, clamp-related risk of stroke remains if partial or side-biting clamps are applied for proximal anastomoses. Others and we have demonstrated that no-touch 'anaortic' approaches avoiding any clamping during off-pump procedures via complete *in situ* grafting result in significantly reduced stroke rates when compared with partial clamping. Therefore, OPCAB *in situ* grafting has been proposed as the 'standard of care' to reduce neurological complications. However, this technique may not be applicable to for every patient as the use of free grafts (arterial or venous) requiring proximal anastomosis is often still necessary to achieve complete revascularization. In these situations, proximal anastomosis can be performed without a partial clamp by using the HEARTSTRING device, and over the last few years, considerable evidence has arisen supporting the impact of HEARTSTRING-enabled anastomosis to significantly minimize atheroembolism and neurological complications when compared with partial- or side-bite clamping. This paper provides a systematic overview and technical information about the combination of OPCAB and clampless strategies using the HEARTSTRING for proximal anastomosis to reduce stroke to levels reported for percutaneous coronary intervention.

Keywords: Coronary artery bypass grafting • Coronary artery disease • Off-pump • Clampless • HEARTSTRING • No-touch • Stroke • Neurological complication

INTRODUCTION

Surgical revascularization remains the gold standard treatment for patients with complex three-vessel coronary artery disease, left main coronary artery involvement or diabetes mellitus [1, 2]. Landmark trials published during the last years provide strong confirmation for the superiority of coronary artery bypass grafting (CABG) over percutaneous coronary intervention (PCI) for long-term survival, cardiac events and repeat revascularization [3–5]. However, the significantly higher occurrence of stroke reported for CABG patients compared with PCI is a major concern and often used as an argument against conventional CABG [6].

In the 5-year follow-up of the SYNTAX trial [4], CABG patients fared better than PCI in regard to cardiac death, myocardial infarction (MI), repeat revascularization, the composites of all-cause death/cerebrovascular accident/MI and MACCE. Based on these findings, investigators again concluded that CABG remains the gold standard treatment for patients with moderate and highly complex multivessel disease (elevated Syntax score); PCI was reserved as an alternative for the minority of patients with the least complex disease (low Syntax score). In addition, the recent FREEDOM trial results demonstrated 5-year superiority for CABG

in diabetic patients across all degrees of lesion complexity [3]. Diabetic patients who underwent CABG had significantly better outcomes than those who underwent PCI on death, MI and the composite of death/MI/stroke. Recommendations that consent be obtained in a heart team setting from all diabetic CAD patients, followed the publication of these results [6]. In regard to long-term outcomes, the ASCERT trial tracked 86 244 CABG patients and 103 549 PCI patients over age 65 with two- or three-vessel disease not requiring emergency treatment by linking the Society of Thoracic Surgery (STS) Adult Cardiac Surgery and American College of Cardiology Foundation databases [5]. Consistent with the SYNTAX and FREEDOM trials, 4-year mortality was significantly lower for CABG than PCI. Furthermore, this long-term survival advantage persisted among patients whose propensity scores were most consistent with the selection for PCI.

Despite the significant advantages in long-term event-free survival highlighted by these reports, higher stroke rates at one year were cited as a significant limitation for CABG in both SYNTAX (2.2 vs 0.6%; $P = 0.003$) and FREEDOM (5.2 vs 2.4%, $P = 0.03$) trials. While stroke rates did not significantly differ at 5 years, the higher

1-year rates perpetuate concern about the risk of stroke associated with surgery.

Recent meta-analyses have also reported elevated stroke rates for CABG vs PCI. The most recent and largest meta-analysis to date [7], consisting of 19 randomized trials across 10 994 patients, concluded that 30-day stroke was almost three times more common with CABG than PCI [1.20 vs 0.34%; odds ratio (OR) 2.94; 95% confidence interval (CI), 1.69–5.09; $P < 0.0001$]. An accompanying examination of outcomes in 33 980 patients from 27 observational studies led researchers to conclude that the higher CABG stroke rate observed in randomized studies was representative of real-world outcomes.

THE OVERALL VALUE OF OFF-PUMP CORONARY ARTERY BYPASS

In parallel to conventional CABG techniques, off-pump coronary artery bypass grafting (OPCAB) without cardiopulmonary bypass (CPB) has evolved during the past 20 years and is slowly gaining acceptance and popularity in numerous centres worldwide. However, the truth being, except selected specialist centres performing >90% cases in an OPCAB fashion, the adoption of OPCAB has been very limited around the globe and accounts for only ~20% of the current practice in the USA and Europe [8,9].

Meta-analyses of randomized controlled trials in low-risk patients display comparable results for both approaches with regard to mortality, MI, and need for repeat revascularization at 1 and 2 years. They also demonstrate OPCAB to be associated with reduction of stroke, wound infection, renal and respiratory complications [9–11]. Next, OPCAB appears to reduce the need for transfusion, inotropic support, ventilation time, the length of hospital stay, and in-hospital and 1-year direct costs [8]. These data were confirmed recently in a large meta-analysis including 35 propensity score analyses with a total of 123 137 patients. This study detected an overall OR <1 for all outcome parameters in favour of OPCAB. These results were significant for most of the evaluated outcome parameters, in particular mortality, suggesting OPCAB to be the superior technique when compared with CABG [12].

In contrast, the ROOBY trial showed a 30% risk increase for the occurrence of the primary composite endpoint including death, MI and need for repeat revascularization after OPCAB [13]. However, this prospective randomized multicentre trial displayed several major limitations, as >70% of the evaluated patients were excluded due to clinical reservations of surgeons who accepted participation in the study after they had performed only 20 OPCAB procedures. This lack of experience was also highlighted by the up to 10-fold higher need for conversion to on-pump (12%), when compared with specialized OPCAB centres that report conversion rates ranging from 1 to 5% [14]. More than 50% of OPCAB patients received transfusions vs only 30% reported in previous randomized trials, and only a small proportion of the cohort were high-risk patients, the suggested subgroup to benefit more likely from OPCAB. And finally only a good team approach with experienced anesthesiologists will yield good results for OPCAB.

WHO ARE THE TARGET PATIENTS FOR OFF-PUMP CORONARY ARTERY BYPASS?

Observational studies suggest that OPCAB is particularly beneficial for high-risk patients, including those with left ventricle dysfunction,

high calcific load, age older than 75 years, diabetes, renal failure, left main stem disease, reoperations, chronic pulmonary disease and an overall EuroSCORE >5 [10–12, 15–19]. In contrast, in the prospective Best Bypass Surgery trial, Moller *et al.* [20] compared outcomes in 341 patients that were randomly assigned to either on-pump or off-pump surgery. At 3 years, this trial did not detect any significant differences with regards to MACCE. However, to date, there is only one multicentre, prospective randomized trial available comparing OPCAB vs on-pump in high-risk patients, whereas at least two trials are underway to evaluate the potential benefit of OPCAB in this subset of patients. The CRISP trial conducted by both the Oxford and Bristol Cardiac Surgery Unit is an international randomized multicentre trial aiming for >5000 high-risk patients with an inclusion criterion of a EuroSCORE >5. Recently, the German Off-Pump Coronary Artery Bypass in Elderly Study (GOPCABE), a multicentre trial randomly assigning 2539 patients older than 75 years to undergo either OPCAB or on-pump, concluded that no significant difference in regard to neurological outcomes was seen. The stroke rate of 2.2% in the OPCAB is, however, very high, but no information on aortic techniques was provided to the reader [21].

STROKE REDUCTION WITH OFF-PUMP CORONARY ARTERY BYPASS

Reports of inferior neurological outcomes for CABG vs PCI have primarily resulted from studies in which conventional on-pump CABG (ONCAB) techniques were used, rather than OPCAB, aortic no-touch strategies or the combination of both. In the SYNTAX trial, only 15% of the patients underwent OPCAB and in the FREEDOM trial, use of cardiopulmonary bypass was left to the surgeon's discretion, with the result that only 20% patients underwent off-pump surgery [3].

There is a compelling body of evidence that OPCAB significantly reduces cerebrovascular complications [22–24]. A propensity-matched analysis of 30-day outcomes in >42 477 consecutive primary isolated CABG patients in the STS Adult Cardiac Surgery database documented a 35% reduction in stroke for OPCAB compared to conventional CABG (OR 0.65, $P = 0.001$) [25]. A 2012 meta-analysis of 59 randomized controlled trials encompassing 8961 patients [26] documented a 30% reduction in the risk of post-operative stroke with OPCAB vs ONCAB [1.4 vs 2.1%; relative risk (RR) 0.70, 95% CI 0.49–0.99]. An analogous meta-analysis of 35 propensity-adjusted observational studies across a total of 123 137 patients [12] detected a significant reduction in stroke with OPCAB (OR 0.42; 95% CI 0.33–0.54; $P < 0.0001$).

ADDITIONAL STROKE REDUCTION WITH CLAMPLESS OFF-PUMP CORONARY ARTERY BYPASS

By eliminating aortic manipulation and cross-clamping required for cardiopulmonary bypass, OPCAB results in a lower incidence of stroke compared with conventional CABG. However, significant clamp-related risk of stroke remains if partial or side-biting clamps are used during the construction of proximal anastomoses. 'Anaortic' approaches avoiding any clamping during off-pump procedures via complete *in situ* grafting (double internal mammary artery and/or T- or Y-grafting) have resulted in stroke

rates that are significantly lower than both conventional CABG and OPCAB with partial clamping.

A 2011 meta-analysis of seven observational studies compared clampless OPCAB with conventional CABG and OPCAB with the use of partial clamp [22]. Avoidance of clamping during OPCAB was associated with a significant reduction in risk of stroke compared with conventional CABG (0.38 vs 1.87% RR 0.27; 95% CI 0.14–0.58; $P < 0.0001$) as well as compared with OPCAB using a partial clamp (0.31 vs 1.35%; RR 0.34; CI 95% 0.18–0.65; $P = 0.001$). A similar meta-analysis of eight studies and 11 398 patients compared neurological complications in off-pump surgery conducted with and without aortic manipulation [27]. Postsurgical neurological complications were reduced by half in aortic OPCAB grafting cases (OR 0.46; 95% CI, 0.29–0.72; $P = 0.008$).

Halbersma *et al.* [28] recently compared 4-year outcomes in 400 consecutive no-touch total arterial OPCAB patients with results in the surgical arm of the SYNTAX trial. There was a clear trend towards a reduction in the event rate of stroke in the no-touch group (0.8%) compared with the surgical arm of the SYNTAX trial (2.2%). Further, there was no significant difference of stroke rate between the no-touch OPCAB group and the PCI arm of the SYNTAX trials.

Based on these results, Halbersema *et al.* [28] and others [22, 24] have proposed off-pump in situ grafting as the 'standard of care' to reduce neurological complications. However, this approach may not be applicable for every patient or in every surgical setting. In many cases to obtain complete revascularization, the use of free grafts (arterial or venous) requiring proximal anastomosis is necessary. In these situations, proximal anastomosis can be performed without a partial clamp by using the HEARTSTRING Proximal Seal System (MAQUET, San Jose, CA, USA).

HEARTSTRING-ENABLED CLAMPLESS PROXIMAL ANASTOMOSIS

The HEARTSTRING Proximal Seal System consists of a specialized aortic cutter, a delivery device and the proximal seal. First, we recommend that the delivery device be bathed for a couple of seconds in warm saline to ensure smooth deployment. We do not use epi-aortic scanning, the aorta can be prepared for a side bite clamping (preventative measure), then identification of anastomotic site is done and the adventitia is prepared. The insertion of a swab between the aorta and the right pericardial reflection will

help with the exposure for the anastomosis. The graft is prepared for suturing to the aorta, and a mean arterial blood pressure of <70 mmHg is achieved. Then, a circular aortotomy is made by using the aortic cutter. Once the hole is made, it is covered with the fingertip to prevent uncontrolled spurting of blood. In the next step, the proximal seal is delivered into the aorta through the hole. To make this manoeuvre easier, we recommend slight rotational movements of the device until a true penetration of the ventral wall is felt. While retracting the sheath with one hand, the other is used to stabilize the HEARTSTRING device during this maneuver. After the seal system is unfolded within the aorta, the proximal anastomosis can be performed within the sealed area (Fig. 1). A fine tip sucker is mandatory to keep the operation field bloodless. When the anastomosis is finished, the seal system is removed with a specially designed removal mechanism.

Over the last few years, considerable evidence has accrued supporting the impact of HEARTSTRING in significantly minimizing atheroembolism and neurological complications compared with partial- or side bite clamping. Guerrieri Wolf *et al.* [29] documented a significant reduction in the proportion of particulate emboli with HEARTSTRING vs partial clamp using transcranial Doppler monitoring of the middle cerebral artery in a prospective study of patients with undocumented degrees of aortic disease. A randomized study from Emory University showed a significant reduction in particulate emboli with HEARTSTRING in patients at low risk for atheroembolism; in patients with no or minimal (Class I and II) aortic disease, HEARTSTRING was associated with a 35% reduction in solid emboli compared with the partial clamp [30].

Additional evidence that use of HEARTSTRING to avoid aortic side-clamping during OPCAB reduces stroke comes from several reported series. Hilker *et al.* [30] performed 542 proximal anastomoses off-pump using the HEARTSTRING device in 412 consecutive patients. Previous neurological disorders or cerebrovascular diseases were documented in 15% of patients. The overall incidence of postoperative stroke was 0.48% in contrast to a 1.3% predicted stroke risk score.

Douglas and Spaniol [31] reported a stroke rate of 0.8% for patients who underwent CABG off-pump with the replacement of partial clamping by HEARTSTRING in patients with severe aortic disease identified using epi-aortic ultrasound. The authors stressed the role of clampless OPCAB as an important tool for the prevention of postoperative stroke and also concluded that adjunctive

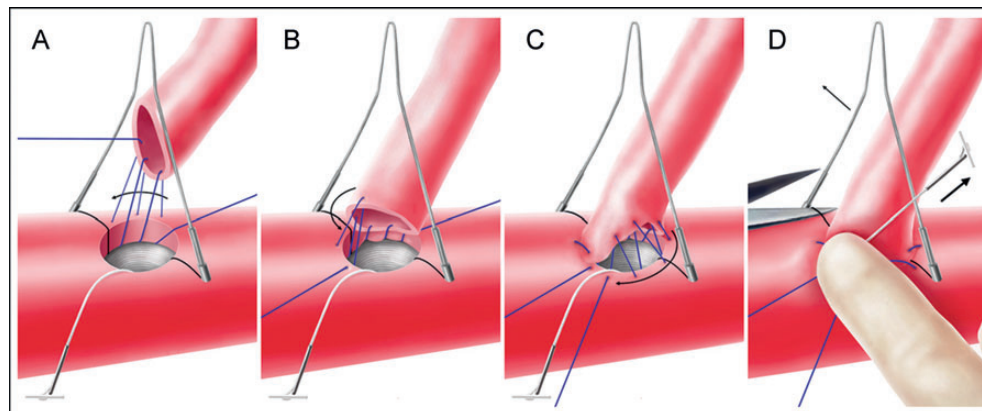


Figure 1: HEARTSTRING-enabled technique for proximal anastomosis. Digital palpation is performed to identify a soft (non-calcified) segment of aorta. Thereafter, the adventitial tissue is mobilized, and cauterized to expose the media. Then a circular aortotomy is created using the aortic-punch device before the coiled HEARTSTRING is inserted. The anastomosis is then performed with a continuous 6-0 Prolene RB suture, a blower/mister or fine tip cell saver is necessary to provide a bloodless field and allow for precise transmural bites. After completion of the anastomosis and before tightening of the suture, the device is removed.

techniques for patients with significant atherosclerosis is likely to have been a major factor in reducing the occurrence of stroke.

Finally, a recent propensity-matched analysis of 4314 patients comparing aortic cross-clamping during conventional on-pump surgery vs partial clamping in OPCAB vs a clampless strategy using the HEARTSTRING device showed that the occurrence of stroke and MACCE can be significantly reduced by using the HEARTSTRING device, yielding results similar to those that can be achieved with no-touch total arterial *in situ* grafting [18]. Importantly, there was no difference in the rate of stroke between patients who underwent a conventional on-pump approach with aortic cross-clamping and patients who received off-pump surgery in combination with partial clamping for proximal anastomosis, suggesting that it is not the type of clamping, but clamping itself, which is an independent predictor for an increased risk of stroke [19].

CONCLUSION

Neurological outcomes are critical in the ongoing debate between interventional and surgical treatment of CAD. The combination of OPCAB and clampless strategies either using complete *in situ* grafting techniques or clampless devices such as HEARTSTRING for proximal anastomosis reduces stroke to levels comparable with PCI. OPCAB in combination with no-touch or HEARTSTRING-enabled proximal anastomotic techniques represent a significant advance over conventional on-pump CABG by achieving the benefits of surgical revascularization with less morbidity and comparable neurological complications as reported for PCI.

Conflict of interest: Sacha Salzberg is a consultant for Maquet.

REFERENCES

- [1] Kolh P, Wijns W, Danchin N, Di Mario C, Falk V, Folliguet T *et al.* Guidelines on myocardial revascularization. *Eur J Cardiothorac Surg* 38 (Suppl):S1–S52.
- [2] Wijns W, Kolh P, Danchin N, Di Mario C, Falk V, Folliguet T *et al.* Guidelines on myocardial revascularization. *Eur Heart J* 31:2501–55.
- [3] Farkouh ME, Domanski M, Sleeper LA, Siami FS, Dangas G, Mack M *et al.* Strategies for multivessel revascularization in patients with diabetes. *N Engl J Med* 2012;367:2375–84.
- [4] Mohr FW, Morice MC, Kappetein AP, Feldman TE, Stähle E, Colombo A *et al.* Coronary artery bypass graft surgery versus percutaneous coronary intervention in patients with three-vessel disease and left main coronary disease: 5-year follow-up of the randomised, clinical SYNTAX trial. *Lancet* 2013;381:629–38.
- [5] Weintraub WS, Grau-Sepulveda MV, Weiss JM, O'Brien SM, Peterson ED, Kolm P *et al.* Comparative effectiveness of revascularization strategies. *N Engl J Med* 2012;366:1467–76.
- [6] Hlatky MA. Compelling evidence for coronary-bypass surgery in patients with diabetes. *N Engl J Med* 2012;367:2437–8.
- [7] Palmerini T, Biondi-Zoccai G, Reggiani LB, Sangiorgi D, Alessi L, De Servi S *et al.* Risk of stroke with coronary artery bypass graft surgery compared with percutaneous coronary intervention. *J Am Coll Cardiol* 2012;60:798–805.
- [8] Lattouf OM, Thourani VH, Kilgo PD, Halkos ME, Baio KT, Myung R *et al.* Influence of on-pump versus off-pump techniques and completeness of revascularization on long-term survival after coronary artery bypass. *Ann Thorac Surg* 2008;86:797–805.
- [9] Patel NN, Angelini GD. Off-pump coronary artery bypass grafting: for the many or the few? *J Thorac Cardiovasc Surg* 2010;140:951–3 e1.
- [10] Puskas JD, Thourani VH, Kilgo P, Cooper W, Vassiliades T, Vega JD *et al.* Off-pump coronary artery bypass disproportionately benefits high-risk patients. *Ann Thorac Surg* 2009;88:1142–7.
- [11] Puskas JD, Kilgo PD, Lattouf OM, Thourani VH, Cooper WA, Vassiliades TA *et al.* Off-pump coronary bypass provides reduced mortality and morbidity and equivalent 10-year survival. *Ann Thorac Surg* 2008;86:1139–46; discussion 46.
- [12] Kuss O, von Salviati B, Borgermann J. Off-pump versus on-pump coronary artery bypass grafting: a systematic review and meta-analysis of propensity score analyses. *J Thorac Cardiovasc Surg* 140:829–35, 35 e1–13.
- [13] Shroyer AL, Grover FL, Hattler B, Collins JF, McDonald GO, Kozora E *et al.* On-pump versus off-pump coronary-artery bypass surgery. *N Engl J Med* 2009;361:1827–37.
- [14] Reeves BC, Ascione R, Caputo M, Angelini GD. Morbidity and mortality following acute conversion from off-pump to on-pump coronary surgery. *Eur J Cardiothorac Surg* 2006;29:941–7.
- [15] Emmert MY, Salzberg SP, Cetina Bieffer HR, Sundermann SH, Seifert B, Grunenfelder J *et al.* Total arterial off-pump surgery provides excellent outcomes and does not compromise complete revascularization. *Eur J Cardiothorac Surg* 41:e25–31.
- [16] Emmert MY, Salzberg SP, Seifert B, Scherman J, Plass A, Starck CT *et al.* Clampless off-pump surgery reduces stroke in patients with left main disease. *Int J Cardiol*.
- [17] Emmert MY, Salzberg SP, Seifert B, Schurr UP, Hoerstrup SP, Reuthebuch O *et al.* Routine off-pump coronary artery bypass grafting is safe and feasible in high-risk patients with left main disease. *Ann Thorac Surg* 2010;89:1125–30.
- [18] Emmert MY, Salzberg SP, Seifert B, Rodriguez H, Plass A, Hoerstrup SP *et al.* Is off-pump superior to conventional coronary artery bypass grafting in diabetic patients with multivessel disease? *Eur J Cardiothorac Surg* 2011;40:233–9.
- [19] Emmert MY, Seifert B, Wilhelm M, Grunenfelder J, Falk V, Salzberg SP. Aortic no-touch technique makes the difference in off-pump coronary artery bypass grafting. *J Thorac Cardiovasc Surg* 2011;142:1499–506.
- [20] Moller CH, Perko MJ, Lund JT, Andersen LW, Kelbaek H, Madsen JK *et al.* Three-year follow-up in a subset of high-risk patients randomly assigned to off-pump versus on-pump coronary artery bypass surgery: the Best Bypass Surgery trial. *Heart* 2011;97:907–13.
- [21] Diegeler A, Borgermann J, Kappert U, Breuer M, Boning A, Ursulescu A *et al.* Off-pump versus on-pump coronary-artery bypass grafting in elderly patients. *N Engl J Med* 2013;368:1189–98.
- [22] Edelman JJ, Yan TD, Bannon PG, Wilson MK, Vallely MP. Coronary artery bypass grafting with and without manipulation of the ascending aorta—a meta-analysis. *Heart Lung Circ* 2011;20:318–24.
- [23] Polonsky M, Puskas JD. Off-pump coronary artery bypass grafting—the current state. *Circ J* 2012;76:784–90.
- [24] Edelman JJ, Sherrah AG, Wilson MK, Bannon PG, Brereton RJ, Ross DE *et al.* Anaortic, total-arterial, off-pump coronary artery bypass surgery—Why bother? *Heart Lung Circ* 2012.
- [25] Puskas JD, Edwards FH, Pappas PA, O'Brien S, Peterson ED, Kilgo P *et al.* Off-pump techniques benefit men and women and narrow the disparity in mortality after coronary bypass grafting. *Ann Thorac Surg* 2007;84:1447–54; discussion 54–6.
- [26] Afilalo J, Rasti M, Ohayon SM, Shimony A, Eisenberg MJ. Off-pump vs. on-pump coronary artery bypass surgery: an updated meta-analysis and meta-regression of randomized trials. *Eur Heart J* 2012;33:1257–67.
- [27] Misfeld M, Brereton RJ, Sweetman EA, Doig GS. Neurologic complications after off-pump coronary artery bypass grafting with and without aortic manipulation: meta-analysis of 11,398 cases from 8 studies. *J Thorac Cardiovasc Surg* 2011;142:e11–7.
- [28] Halbersma WB, Arrigoni SC, Mecozzi G, Grandjean JG, Kappetein AP, van der Palen J *et al.* Four-year outcome of OPCAB no-touch with total arterial Y-graft: making the best treatment a daily practice. *Ann Thorac Surg* 2009;88:796–801.
- [29] Guerrieri Wolf L, Abu-Omar Y, Choudhary BP, Pigott D, Taggart DP. Gaseous and solid cerebral microembolization during proximal aortic anastomoses in off-pump coronary surgery: the effect of an aortic side-biting clamp and two clampless devices. *J Thorac Cardiovasc Surg* 2007;133:485–93.
- [30] Hilker M, Arlt M, Keyser A, Schopka S, Klose A, Diez C *et al.* Minimizing the risk of perioperative stroke by clampless off-pump bypass surgery: a retrospective observational analysis. *J Cardiothorac Surg* 2010;5:14.
- [31] Douglas JM Jr., Spaniol SE. A multimodal approach to the prevention of postoperative stroke in patients undergoing coronary artery bypass surgery. *Am J Surg* 2009;197:587–90.
- [32] Puskas JD, Williams WH, Duke PG, Staples JR, Glas KE, Marshall JJ *et al.* Off-pump coronary artery bypass grafting provides complete revascularization with reduced myocardial injury, transfusion requirements, and length of stay: a prospective randomized comparison of two hundred unselected patients undergoing off-pump versus conventional coronary artery bypass grafting. *J Thorac Cardiovasc Surg* 2003;125:797–808.